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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/669,158	09/22/2003	Edward A. Neuwelt	720109.401	1678

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EXAMINER	
ARNOLD, ERNST V	
ART UNIT	PAPER NUMBER
1616	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/12/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/669,158	NEUWELT ET AL.	
	Examiner	Art Unit	
	Ernst V. Arnold	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 February 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-19 and 21-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-19 and 21-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 2 and 20 have been cancelled. Claims 1, 3-19 and 21-25 are pending. The Examiner acknowledges receipt of Applicant's remarks filed on 2/5/07. Applicant's amendment has necessitated a new ground of rejection. This action is FINAL.

Comment: In claim 4, ethyol® is a registered trademark name and should be replaced with amifostine.

Withdrawn rejections:

Claims 1, 3-19 and 21-25 were rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a reducing an ischemia-reperfusion injury, does not reasonably provide enablement for preventing an ischemia-reperfusion injury. Applicant has amended the claims to read on a method of reducing an ischemia-reperfusion injury. The Examiner withdraws the rejection.

Claims 1, 3-7, 14, 15, 17, 18, 24 and 25 were rejected under 35 U.S.C. 102(b) as being anticipated by Singh (5,912,019). Applicant has amended claim 1 to recite a specific serum concentration of at least 1.5 mM of the free radical scavenger. Singh does not disclose a serum concentration of at least 1.5 mM and the Examiner withdraws the rejection.

Claims 1, 3-19 and 21-25 were rejected under 35 U.S.C. 103(a) as being unpatentable over Singh (5,912,019) in view of Andersen (Perfusion 1995, 10, 21-26). Applicant has amended claim 1 to recite a specific serum concentration of at least 1.5

mM of the free radical scavenger. Singh does not disclose a serum concentration at this level and Andersen does not cure this deficiency. The Examiner withdraws the rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 24 and 25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is unclear to the Examiner the metes and bounds of "at least about". It is unclear to the Examiner which of the terms is the limiting term. One indicates a defined bound but the other indicates leeway. The Examiner will interpret the claim as reading on "about".

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1, 2-19 and 21-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Singh (5,912,019) in view of Andersen (Perfusion 1995, 10, 21-26) and Koeppel et al. (Transplantation 1996, 61(9), 1397-402.

Applicant claims a method for reducing an ischemia-reperfusion injury.

Determination of the scope and content of the prior art

(MPEP 2141.01)

Singh teaches methods of minimizing ischemic insult to an organ or skeletal tissue of a subject comprising contacting the organ or tissue with an inhibitor of iNOS (N-acetyl-cysteine) (Claims 1 and 2). Singh teaches that animals were treated with N-acetyl-cysteine before and after the onset of ischemia (Column 7, liens 35-41). Singh teaches that the method can be performed intraarterial, intravenous, subcutaneous or intramuscular injections (column 5, lines 60-65). Singh teaches that a preferred dosage is from about 100 to about 300 mg/kg body weight (Column 5, lines 39-42). Singh teaches that the method may also be used where ischemic conditions are induced by infarctions and it is the Examiner's position that the infarct size would be reduced (Column 4, lines 55-57). Singh defines organ as including the brain and thus reads on claim 7. It is the Examiner's position that the blood will carry the scavenger to the central nervous system 18.

Andersen teaches the role of N-acetylcysteine administration during cardiopulmonary bypass (Abstract). Andersen teaches that patients received a bolus of 100 mg/kg N-acetylcysteine followed by a continuous infusion of 20 mg/kg via the reservoir of the bypass circuit from the beginning to the end of the cardiopulmonary bypass (Page 22, Patients and methods). Andersen teaches that N-acetylcysteine may be used safely alone or in conjunction with other therapies, which aim to minimize reperfusion injuries (Page 26, second paragraph).

Koeppel et al. teach administration of 400 mg/kg N-acetylcysteine to Lewis rats and "conclude that high-dose therapy with N-acetylcysteine in orthotopic liver transplantation attenuates manifestations of microvascular perfusion failure early after reperfusion and should be considered as a means to reduce reperfusion injury." (Abstract).

Ascertainment of the difference between the prior art and the claims (MPEP 2141.02)

1. Singh do not expressly teach a serum concentration of the free radical scavenger of at least 1.5 mM.

2. Singh does not expressly teach a method for reducing an ischemia-reperfusion injury, wherein the ischemia-reperfusion injury is a cerebral injury, cognitive dysfunction or cerebral hemorrhage.

3. Singh does not expressly teach a method for reducing an ischemia-reperfusion injury, wherein the ischemia-reperfusion injury is associated with cardiopulmonary bypass procedure.

Finding of prima facie obviousness

Rational and Motivation (MPEP 2142-2143)

1. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to increase the dosage of N-acetylcysteine to 400 mg/kg, as suggested by Koeppel et al., in the method of Singh and produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because Singh teaches using *about* 300 mg/kg and the art teaches a high dose treatment of 400 mg/kg, which attenuates manifestations of microvascular perfusion failure. One of ordinary skill in the art would have used the higher dosage suggested by Koeppel et al. as an effective therapeutic amount of the free radical scavenger. Applicant teaches that N-acetylcysteine administered at 400 mg/kg results in serum N-acetylcysteine concentrations of about 1.5 mM (specification page 16, lines 10-13).

2. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to use the method of Singh for reducing an ischemia-repefusion injury, wherein the ischemia-reperfusion injury is a cerebral injury, cognitive dysfunction or cerebral hemorrhage.

One of ordinary skill in the art would have been motivated to do this because Singh teaches that the method may be employed upon occurrences of various traumas to the central nervous system, cerebral hemorrhage, stroke, and temporary occlusion of blood vessels.

3. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to use the method of Singh for reducing an ischemia-repefusion injury wherein the ischemia-reperfusion injury is associated with a cardiopulmonary bypass procedure, as suggested by Andersen, and produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because Andersen teaches the cardiopulmonary bypass results in reperfusion injuries (Page 21, introduction) and the method of Singh would reduce these injuries. The adjustment of particular working conditions (e.g., the method of administration, the time of administration and the amount of the N-acetyl-cysteine administered) is deemed merely a matter of routine optimization which is within the skill of one of ordinary skill in the art.

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (*In re Opprecht* 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA) 1976).

In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of

ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ernst V. Arnold whose telephone number is 571-272-8509. The examiner can normally be reached on M-F (6:15 am-3:45 pm).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Ernst Arnold
Patent Examiner
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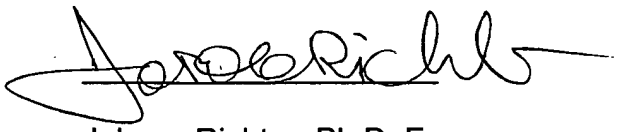

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